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Prevention

=EFFICACY AND SAFETY OF BOCOCIZUMAB (RN316/PF-04950615), A MONOCLONAL ANTIBODY AGAINST PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 IN STATIN-TREATED HYPERCHOLESTEROLEMIC SUBJECTS: RESULTS FROM A RANDOMIZED, PLACEBO-CONTROLLED, DOSE-RANGING STUDY (NCT: 01592240)

Poster Contributions
Hall C
Sunday, March 30, 2014, 9:45 a.m.-10:30 a.m.

Session Title: Prevention: Familial Hypercholesterolemia, Novel Therapies and Cardiovascular Risk
Abstract Category: 20. Prevention: Clinical
Presentation Number: 1183-129

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Background: Bococizumab (BOCO) is a humanized monoclonal antibody that binds to proprotein convertase subtilisin/kexin type 9 and is a therapeutic approach for reducing LDL-C levels in hypercholesterolemic (HC) patients. The objective of this study was to evaluate various BOCO subcutaneous (SC) doses administered every 2 weeks (Q14d) or monthly (Q28d).

Methods: This was a 24-week, multicenter, randomized, double-blind, placebo-controlled trial in statin-treated subjects aged ≥18 yrs with a diagnosis of HC and LDL-C ≥80 mg/dL. Subjects were randomized to Q14d SC placebo, BOCO 50 mg, 100 mg, or 150 mg; or Q28d placebo, BOCO 200 mg or 300 mg. Doses were reduced if LDL-C readings were ≤25 mg/dL. The primary analysis was the placebo-adjusted treatment difference for the change from baseline in LDL-C at Week 12.

Results: BOCO significantly reduced LDL-C across all doses (Table). Up to 44% of subjects in the BOCO groups had their dose reduced. Model-based simulation that assumed no dose reductions predicted greater LDL-C lowering than the primary endpoint, which included subjects having doses reduced. AEs were similar across placebo and BOCO groups. Few subjects discontinued treatment due to treatment-related AEs (Table).

Conclusions: BOCO 150 mg Q14d significantly reduced LDL-C by 53 mg/dL vs. placebo at Week 12, inclusive of the protocol-directed dose reductions in 35% of subjects. Modeling predicted greater LDL-C reduction in absence of BOCO dose reduction. The Q14d regimen is being evaluated in larger trials.

	Placebo Q14d (n=49)	BOCO 50 mg Q14d (n=50)	BOCO 100 mg Q14d (n=51)	BOCO 150 mg Q14d (n=49)	Placebo Q28d (n=51)	BOCO 200 mg Q28d (n=50)	BOCO 300 mg Q28d (n=51)
Baseline LDL-C, mg/dL	108.7 ± 31.5	107.9 ± 20.2	113.4 ± 25.7	105.8 ± 18.0	118.8 ± 44.8	105.7 ± 23.2	104.7 ± 22.1
Subjects with dose reduction	0	0	16%	35%	0	44%	39%
Absolute change from baseline in LDL-C at Week 12, mg/dL	−2.8 ± 29.2	−35.4 ± 26.6	−52.3 ± 31.3	−54.2 ± 27.0	−1.3 ± 37.2	−21.3 ± 28.0	−38.3 ± 41.3
Adjusted change from baseline in LDL-C at Week 12, versus placebo,* mg/dL	---	−34.3 (−45.1, −23.5)	−45.1 (−55.9, −34.2)	−53.4 (−64.1, −42.7)	---	−27.6 (−40.5, −14.7)	−44.9 (−57.7, −32.1)
Model predicted placebo-adjusted LDL-C change from baseline at Week 12 assuming no dose reduction,** mg/dL	---	−36.3 (−42.0, −30.3)	−60.6 (−67.1, −55.5)	−72.1 (−77.5, −67.0)	---	−40.3 (−47.2, −34.3)	−55.7 (−61.6, −48.0)
Subjects with treatment-related SAEs	0	0	0	2%	0	0	0
Discontinuation of treatment due to treatment-related AEs	0	2%	0	8%	0	0	4%

Values are mean ± SD, %, or n=number treated, also see * and ** below. BOCO, bococizumab; LDL-C, low-density lipoprotein cholesterol; AE, adverse event; SAE, serious AE.
*Mean (95% confidence interval), calculated using a repeated measures model for longitudinal data.
**Population PK/PD model predictions of median absolute LDL-C change from baseline (2.5th and 97.5th percentile) for 100 trials (50 subjects/arm) using baseline demographics observed in this study.